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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/571,662

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Susan P. James

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EXAMINER

KRISHNAN, GANAPATHY

ART UNIT

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1623

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PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/571,662	<b>Applicant(s)</b> JAMES ET AL.	
	<b>Examiner</b> Ganapathy Krishnan	<b>Art Unit</b> 1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 30 March 2006.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-15 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 1-3, 7 and 8 is/are allowed.
- 6) ☒ Claim(s) 4-6, 9, 10 and 12-15 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 10 March 2006 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)          | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____  | 6) <input type="checkbox"/> Other: _____                          |

## **DETAILED ACTION**

### ***Specification***

The first page of the WIPO document filed 31 March, 2005, which has an abstract, has also been used as the abstract sheet in the instant specification. This is not acceptable if the instant claims are determined to be allowable at a later stage. The Office requires the abstract to be typed on a separate sheet of paper even though applicants intend using the abstract on the WIPO document for the instant application. Hence, applicants are requested to kindly type the abstract appearing on the first page of the WIPO document (WO 2005/028632) on a separate sheet and file the same.

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 12 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for hyaluronan esters integrated with specific chemical components such as those as taught in the art recited below (Giusti et al) , does not reasonably provide enablement for the same using any other components as broadly claimed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Undue experimentation is a conclusion reached by weighing the noted factual considerations set forth below as seen in *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400,

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**1404 (Fed. Cir. 1988).** A conclusion of lack of enablement means that, based on the evidence regarding a fair evaluation of an appropriate combination of the factors below, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation.

These factors include:

- (A) The breadth of the claims;
- (B) The nature of the invention;
- (C) The state of the prior art;
- (D) The level of predictability in the art;
- (E) The amount of direction provided by the inventor;
- (F) The existence of working examples; and
- (G) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

#### **The breadth of the claims - The nature of the invention**

Claim 12 is drawn to a regenerated hyaluronan integrated with a component. The ordinary dictionary meaning (Compact Oxford English Dictionary) of the term component is ‘a part or element of a larger whole’. The said term is therefore broad and is seen to include several things in combination with the regenerated hyaluronan.

#### **The state of the prior art**

Prior art Giusti et al (US 5,644,049) teaches several chemical components that can be integrated with hyaluronic acid. Other than such compounds no other components are taught as being usable in combination with regenerated hyaluronic acid.

#### **The level of predictability in the art**

Based on the teachings of the prior art it is highly unpredictable as to what other components can be combined with regenerated hyaluronic acid.

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**The amount of direction provided by the inventor**

The instant specification is not seen to provide adequate guidance that would allow the skilled artisan to extrapolate from the disclosure and examples provided to make the product claimed commensurate in the scope with the instant claim. There is a lack of data and examples that adequately represent the claim as written. Applicants have not provided any indication of what type of components can be combined other than mentioning that regenerated hyaluronan can be combined with polyethylene for making implants (specification, page 9, lines 19-21).

**The existence of working examples**

The examples provided in the instant specification are drawn to esterification of silylated hyaluronic acid ammonium complex, Saponification of hyaluronic acid esters and crosslinking. There are no examples of combination of hyaluronic acid with other components. One of ordinary skill in the art will not extrapolate the teachings in the instant specification and the prior art to combine regenerated hyaluronic acid with any component as broadly encompassed by the recitation in the instant claim.

**The quantity of experimentation needed to make and use the invention based on the content of the disclosure**

Indeed, in view of the information set forth supra, the instant disclosure is not seen to be sufficient to enable one to make and use the combination of the claimed agent and components without undue experimentation. It is noted that the specification should teach how to make and use the invention, not teach how to figure out for oneself how to make and use the invention. See *In re Gardner, 166 USPQ 138 (CCPA 1970)*.

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The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

***Written Description***

Claims 5 and 12 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The instant claims are directed to seeding with animal cells and integration with a component respectively. The specification, at pages 2-3, mentions seeding with cells in general and integrating with components. The genus “cells” is exceedingly large.

The MPEP states that for a generic claim, the genus can be adequately described if the disclosure presents a sufficient number of representative species that encompass the genus. See MPEP § 2163. If the genus has a substantial variance, the disclosure must describe a sufficient variety of species to reflect the variation within that genus. See MPEP § 2163. Although the MPEP does not define what constitute a sufficient number of representative species, the courts have indicated what do not constitute a representative number of species to adequately describe a broad genus. In *Gostelli*, the courts determined that the disclosure of two chemical compounds within a subgenus did not describe that subgenus. *In re Gostelli*, 872, F.2d at 1012, 10 USPQ2d at 1618. Additionally, in *Carnegie Mellon University v. Hoffman-La Roche Inc.*, Nos. 07-1266, - 1267 (Fed. Cir. Sept. 8, 2008), the Federal Circuit affirmed that a claim to a genus described in

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functional terms was not supported by the specification's disclosure of species that were not representative of the entire genus. Furthermore, for a broad generic claim, the specification must provide adequate written description to identify the genus of the claim. In *Regents of the University of California v. Eli Lilly & Co.* the court stated:

"A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *Fiers*, 984 F.2d at 1171, 25 USPQ2d 1601; *In re Smythe*, 480 F.2d 1376, 1383, 178 USPQ 279, 284985 (CCPA 1973) ("In other cases, particularly but not necessarily, chemical cases, where there is unpredictability in performance of certain species or subcombinations other than those specifically enumerated, one skilled in the art may be found not to have been placed in possession of a genus ...") *Regents of the University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398.

The claims are rejected under the written description requirement for failing to disclose any species for the claimed genus, the genus being saccharide.

The Guidelines for Examination of Patent Applications under the 35 USC § 112, first paragraph, "Written Description" Requirement", published at Federal Register, Vol. 66, No. 4, pp. 1099-1111 outline the method of analysis of claims to determine whether adequate written description is present. The first step is to determine what the claim as a whole covers, i.e., discussion of the full scope of the claim. Second, the application should be fully reviewed to understand how applicant provides support for the claimed invention including each element and/or step, i.e., compare the scope of the claim with the scope of the description. Third, determine whether the applicant was in possession of the claimed invention as a whole at the time of filing. This should include the following considerations: (1) actual reduction to practice, (2) disclosure of drawings or structural chemical formulas, (3) sufficient relevant identifying characteristics such as complete structure, partial structure, physical and/or chemical properties and functional characteristics when coupled with a known or disclosed correlation between function and structure, (4) method of making the claimed invention, (5) level of skill and

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knowledge in the art and (6) predictability of the art. For claims 5 and 12, each of these factors have been considered, with the most relevant factors discussed below. For each claim drawn to a genus, each of these factors is to be considered to determine whether there is disclosure of a representative number of species that would lead one skilled in the art to conclude that applicant was in possession of the claimed invention. Where skill and knowledge in the art is high, adequate written description would require fewer species to be disclosed than in an art where little is known; further, more species would need to be disclosed to provide adequate written description for a highly variable genus.

First, what do the claims as a whole cover? Claims 5 and 12 are directed to compounds that have animal cells and components in combination with hyaluronan ester or regenerated hyaluronic acid, which is seen to include anything as a component. Animal cells are a sub-genus of the genus, cells.

Second, how does the scope of the claims compare to the scope of the disclosure? The genus claimed is broader than what is supported in the disclosure. The claims are drawn to compounds having any type of animal cells and component. The disclosure does not provide any examples of such combinations. It just mentions that the hyaluronic acid esters can be further processed, e.g., seeded with cells (specification, page 2, line 13).

Third, the factors to be considered, with the most relevant factors discussed below.

Reduction to Practice: The only compounds reduced to practice are hyaluronic acid esters containing the acyl part as recited in claim 2(b), the regenerated hyaluronic acid from these esters and crosslinking of the regenerated hyaluronic acid.

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Disclosure of Drawings or Structural Chemical Formulas: The only disclosures seen are mention of hyaluronic acid esters of instant invention which can be further processed, e.g., seeded with cells (specification, page 2, line 13; Figure 1, box 38) and Figure 2, showing the structure of the ammonium salt and the silylation step. This is not seen to constitute a written description of every species in the genus, 'cells' because it would not "reasonably lead" those skilled in the art to any other particular species. Therefore, there is no disclosure of species in addition to the above, which have been reduced to practice.

Level of Skill in the Art and Knowledge in the Art: The level of skill in the art is a person with experience in organic synthesis.

Thus, having analyzed the claims with regard to the Written Description guidelines, it is clear that the specification does not disclose a representative number of species for the recitations in the instant claims. Thus, one skilled in the art would be lead to conclude that Applicants were not in possession of the claimed invention at the time the application was filed.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 4, 6 and 9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "substantially" in claim 4 is a relative term which renders the said claim and other claims in which the said term is recited, indefinite. The term "substantially" is not defined by the claim(s), the specification does not provide a standard for ascertaining the requisite

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degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 12-15 are rejected under 35 U.S.C. 102(b) as being anticipated by Giusti et al (US 5,644,049).

Giusti et al. disclose a sponge composition (porous composition, a structure shape as instantly claimed) comprising a hydrophobic polymer host (polyvinylpyrrolidone (PVP)) and hyaluronic acid (see example 14, col. 9, lines 1-24 and abstract. See also other examples in cols. 5-12). In addition, Giusti et al. disclose that such material can be in the form of a film, a membrane, a sponge, a hydrogel, a guide channel, a thread, gauze, or a non-woven tissue. The hyaluronic acid can be a total or partial hyaluronic acid ester or a hyaluronic acid salt (see abstract). The ester or salt can be formed with a pharmacologically active molecule (see abstract). The product of Giusti is seen to read on the instant claims as they are seen to teach structure shapes comprising hyaluronic acid integrated with another component. The hyaluronic acid of the prior art is seen to be the same as the instant hyaluronic acid, which(the instant) is generated by saponification (i.e. hydrolysis of ester groups on the hyaluronic acid).

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Claims 12-15 are Product-by-Process claim. Product-by-Process claims are not limited to the manipulations of the recited steps, only the structure implied by the steps.

“Even though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process.” In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985).

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various

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claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 10-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Giusti et al (US 5,644,049).

. Giusti et al. disclose a sponge composition (porous composition, a structure shape as instantly claimed) comprising a hydrophobic polymer host (polyvinylpyrrolidone (PVP)) and hyaluronic acid (see example 14, col. 9, lines 1-24 and abstract. See also other examples in cols. 5-12). In addition, Giusti et al disclose that such material can be in the form of a film, a membrane, a sponge, a hydrogel, a guide channel, a thread, gauze, or a non-woven tissue. The hyaluronic acid can be a total or partial hyaluronic acid ester or a hyaluronic acid salt (see abstract). The ester or salt can be formed with a pharmacologically active molecule (see abstract). The hyaluronic acid esters of Giusti is useful in the biomedical, and sanitary fields including dermatology, urology, orthopedics, plastic surgery, etc. (col. 2, lines 44-50).

Della Valle, esters of hyaluronic acid, teaches the isopentenyl esters of the same (col. 30, Example 23). According to della Valle such esters possess interesting bio-plastic and pharmaceutical properties and are also more stable to the degradation by natural enzymes (col. 2, lines 52-67). The esters can also be used as vehicles for medicaments (col. 10, line 38 to col. 16, line 25).

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However, both Giusti and della Valle do not specifically teach the use of the esters of hyaluronic acid comprising the hexanoyl and other acyl groups as recited in instant claim 12.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make the esters of hyaluronic acid as instantly claimed since similar structurally closely related esters are seen to be taught in the prior art. One ordinary skill in the art would be motivated to make and use the esters as instantly claimed since the prior art teaches the use of similar esters in biomedical fields due to their interesting bio-plastic and pharmaceutical properties and their stability to enzyme degradation, as taught by Della Valle. Moreover, esterified derivatives of hyaluronic acid have been found to have a greater degree of hydrating the skin (della Valle, col. 41, lines 42-51). One of ordinary skill in the art would look for other ester derivatives that possess such properties.

### ***Conclusion***

1. Claims 4-6, 9-10 and 12-15 are rejected.
2. Claims 1-3 and 7-8, drawn to a process for producing hyaluronan esters involving a silylation step, as instantly claimed is seen not to be taught or fairly suggested by the prior art.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ganapathy Krishnan whose telephone number is 571-272-0654. The examiner can normally be reached on 8.30am-5pm.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia A. Jiang can be reached on 571-272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Shaojia Anna Jiang/  
Supervisory Patent Examiner, Art Unit 1623

/Ganapathy Krishnan/  
Examiner, Art Unit 1623